

Patent Application  
Docket No. INN.123  
Serial No. 10/537,394

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner : Michael J. Teale  
Art Unit : 1614  
Applicants : Francois Romagne, Helene Sicard, Jerome Tiollier, Christian Belmant  
Serial No. : 10/537,394  
Filed : June 2, 2005  
For : Compositions and Methods for Regulating an Immune Response in a Subject

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

DECLARATION OF FRANCOIS ROMAGNE, HELENE SICARD, JEROME TIOLLIER AND  
CHRISTIAN BELMANT UNDER 37 C.F.R. §1.131

Sir:

Francois Romagne, Helene Sicard, Jerome Tiollier and Christian Belmant declare:

1. That we are co-inventors of the invention disclosed and claimed in U.S. Application Serial No. 10/537,394;
2. That said invention was conceived and reduced to practice on, or before, July 8, 2002 (the critical date) in France;
3. That we conceived and reduced to practice methods for treating methods of treating solid tumors, such as renal cell carcinoma, using the claimed compounds, such as 3-(bromomethyl)-3-butanol-1-yl-diphosphate (BrHPP) to induce  $\gamma\delta$  T-cells in and individual having a solid tumor; and

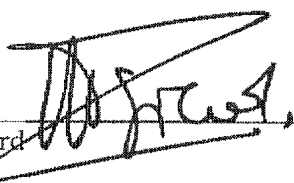
4. That Exhibit 1 contains a copy of a document establishing that the inventors conceived of a method of treating a solid tumors comprising the administration of a composition  $\gamma\delta$  cell activator, such as BrHPP, in a pharmaceutically acceptable carrier and administering such a composition to a subject having a solid tumor (e.g., renal cell carcinoma). Dates and other confidential information have been redacted from the attached exhibit; however, the document and experimental data disclosed therein was prepared on or prior to the critical date of July 8, 2002.

We hereby further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Further, Declarants sayeth not.

By:   
Francois Romangne

Date: 17 Nov. 08

By:   
Helene Sicard

Date: 17 Nov. 08

By:   
Jerome Tollier

Date: 17 Nov 08

By:   
Christian Belmant

Date: 17-Nov-2008

Attachment: Exhibit 1; Laboratory data

# **EXHIBIT 1**

A PHASE I/II DOSE RANGING TOLERANCE STUDY OF INNACELL GD  
IN COMBINATION WITH A FIXED DOSE OF IL-2  
IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA

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<u>PRINCIPAL INVESTIGATOR</u>	[REDACTED] Department : Oncologie Médicale  Centre [REDACTED] Centre [REDACTED] Site Hospitalier [REDACTED]  Tel: [REDACTED] Fax: [REDACTED] e-mail: [REDACTED]
<u>CO-INVESTIGATORS</u>	[REDACTED] [REDACTED] Department : Oncologie Médicale

[REDACTED] Committee  
DATE OF ETHICS COMMITTEE APPROVAL:

Protocol number : [REDACTED]

## TABULATED SYNOPSIS/ OUTLINE PROTOCOL

<b><u>Study title</u></b>	A PHASE III DOSE RANGING TOLERANCE STUDY OF INNACELL GD IN COMBINATION WITH A FIXED DOSE OF IL-2 IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA
<b><u>Investigator site</u></b>	National, monocenter study [REDACTED]
<b><u>Phase</u></b>	III
<b><u>Indication</u></b>	Metastatic Cell Renal Carcinoma
<b><u>Objectives</u></b>	<ul style="list-style-type: none"><li>Primary: Determination of the tolerance of escalating doses of INNACELL GD alone and in combination with a fixed dose of IL-2 in patients with metastatic renal cell carcinoma (MRCC).</li><li>Secondary: Biological effect assessment of the co-treatment with IL-2 evaluated [REDACTED] by immunomonitoring [REDACTED]</li></ul>
<b><u>Study design</u></b>	<p>Open, non randomized phase III study</p> <p>The study consists of [REDACTED] infusions [REDACTED] of INNACELL GD, [REDACTED]</p> <ul style="list-style-type: none"><li>[REDACTED]</li><li>[REDACTED]</li></ul> <p>A classical clinical phase I dose escalating scheme has been designed.</p> <p>[REDACTED]</p> <p>[REDACTED]</p>

<u>Study population</u>	[REDACTED]
<u>Sample Size</u>	10 to 16 patients - [REDACTED]
<u>Study treatment</u>	<p>INNACELL GD is manufactured <i>in vitro</i> from an autologous mononuclear cell preparation, after a single stimulation by BrHPP [REDACTED] [REDACTED] [REDACTED]</p> <ul style="list-style-type: none"><li>- [REDACTED]</li><li>- [REDACTED]</li><li>- [REDACTED]</li><li>- [REDACTED]</li><li>- [REDACTED]</li></ul>

[REDACTED] [REDACTED]